Variations in the Natural History of Psoriasis

EUGENE M. FARBER, M.D., and JOSEPH B. PETERSON, M.D., Palo Alto

• **Latent psoriasis is a state which exists before the development of clinical psoriasis and wherein probably some as yet undiscovered defect exists. Investigation concerning a group of persons with latent psoriasis might disclose basic aberrations.**

The natural course of psoriasis may be altered by therapy. Folic acid antagonists and intradermal corticosteroids may at times eclipse psoriatic lesions. Oral adrenal corticosteroids may prove morbidistatic but on discontinuance a rebound flare may occur which is both protracted and recalcitrant. Antimalarial agents when employed as therapy for coexistent arthridites may cause psoriasis to become more severe.

The Goeckerman regimen which employs topical tar and ultraviolet light therapy produces in some 75 per cent of patients a prolonged remission. As it is safe and repeatable it is favored for the usual severe case of psoriasis.

Psoriasis therapy is better assessed by considering its effect on the natural evolution of the disease.

PSORIASIS is a common disease of unknown cause. Many modes of therapy have been advocated in the management of this frequently recalcitrant disease. The purpose of this report is to evaluate the natural course of psoriasis in order that the effects of therapeutic agents may be assessed in proper perspective.

Psoriasis is uncommon before the age of ten years and rare before the age of three years. It has been noted shortly after birth[8] but may not appear until 80 years of age. There is no difference in sex incidence. Different types are delineated largely on the basis of morphologic variations. Standard texts describe such forms as geographic, eczematous, rupoid, guttate, pustular, exfoliative and seborrheic.[11] While the usually stated incidence of psoriasis is approximately one and a half to two per cent, the actual incidence is probably somewhat higher, perhaps from 3 to 4 per cent of the population. The higher proportion is more probable when one includes persons with a psoriatic diathesis in whom actual clinical evidence is present for perhaps only one or two short periods, or who perhaps do not show clinical evidence of the disease but might if certain stimuli were brought to bear.

It is helpful for a better understanding of psoriasis if we postulate the existence of a latent phase. This phase may start at birth or possibly later. During this period there is no clinical manifestation of psoriasis, but there may be some aberration already present. Clinical psoriasis emerges from the latent phase regardless of the age at which it appears. Initially the evidence for psoriasis may be only a solitary small asymptomatic patch, or it may appear suddenly in widespread areas. Once clinical psoriasis develops, it may show wide variation in severity but it generally remains clinically evident. Complete remission is not common, but it may occur and it signifies that the patient once again has entered a latent phase.

Stimuli, one or more of which will result in the emergence of "clinical" psoriasis from the "latent" state, are usually the same factors that aggravate clinical psoriasis. One such factor is that of seasonal variation, which has long been known to affect psoriasis. Thus clinical psoriasis may become aggravated or first appear during the winter (Chart 1).

Clinical psoriasis may initially appear following a laceration. Similarly it may appear in the laceration site of previously uninvolved skin in a person with clinical psoriasis (Chart 2). This is an example of the so-called isomorphic or Köebner response[5] in which dermal injury incites a response of psoriasis in the injured area. Acute sunburn, the irritant effect of adhesive tape, and numerous other stimuli can "trigger" this response in psoriasis. Stressful circumstances (Chart 3) have repeatedly been observed to coincide with the initial evidence of psoriasis and to aggravate preexisting psoriasis.

A gain in weight is deleterious in that it increases the extent and severity of psoriasis (Chart 4). In

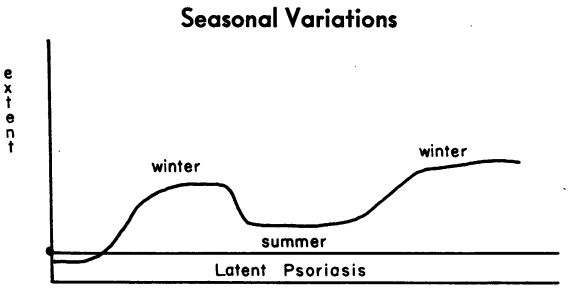

Chart 1.—Natural history of psoriasis. There are alterations in psoriasis corresponding to seasonal change.

From the Department of Dermatology, Stanford University School of Medicine, Palo Alto.

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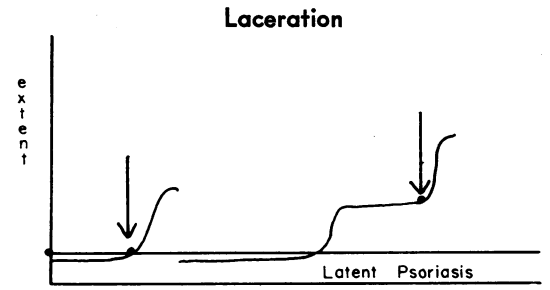

Chart 2.—Natural history of psoriasis. Koebner response to laceration. As shown, this may result in initial appearance of psoriasis, or in a new plaque in preexisting clinical psoriasis.

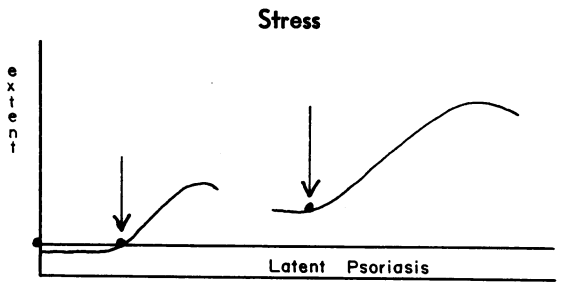

Chart 3.—Stress may either initiate or aggravate psoriasis.

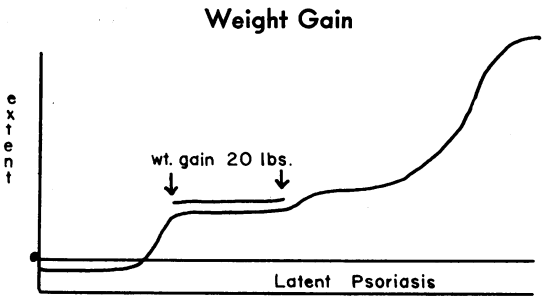

Chart 4.—Aggravation of existing psoriasis by excessive weight gain in a two-month period.

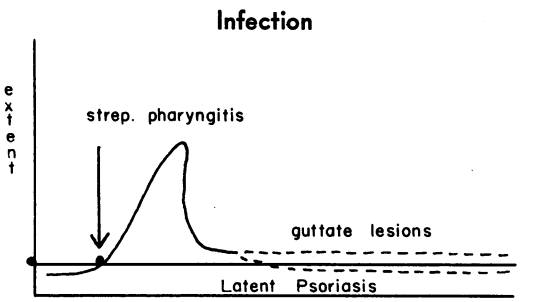

Chart 5.—Initial psoriasis following acute streptococcal infection in patient ten years of age.

approximately 10 per cent of patients the initial psoriatic lesions develop following or coincident with excessive increase in weight.[3] This is analogous to the situation in which diabetes mellitus becomes clinically manifest following a gain in body weight. Similarly both clinical diabetes and clinical psoriasis may regress to subclinical or latent phases upon reduction of the body weight. In either instance the abnormal physiological pattern is probably "under cover" and having the potential to again manifest itself in a recognizable form.

Acute streptococcal infections such as otitis media, pharyngitis, and cellulitis not infrequently herald the initial clinical manifestations of psoriasis[9,10] (Chart 5). The eruption so induced is often explosive in onset and consists of minute droplet-like patches over the entire body. Psoriasis of this type may resolve rapidly and even completely, or it may linger in several sites for an indefinite time following the eradication of the infection.

While the factors of season, weight gain, infection, dermal injury and stress are well authenticated, there are doubtless other as yet incompletely understood natural factors which influence the course of untreated psoriasis. Hormonal, genetic, and environmental aspects are of great influence but need more elucidation.

Delineation of the concept of latent psoriasis is not yet supported by biochemical evidence. Nonetheless it is fair to speculate that a person with latent psoriasis may well have biochemical aberrations long before the appearance of initial clinical psoriasis. The surface skin fat from uninvolved skin areas of patients with psoriasis has a decreased esterified cholesterol level[15] and such skin areas also have an abnormal sterol present in the epidermal lipid.[14] It may well be that these changes are to be found in latent psoriasis. Analysis of psoriatic scales shows large amounts of both ribose and uracil as breakdown products of ribonucleic acid.[17] It is possible that skin scrapings from persons with latent psoriasis would show such changes. There are a number of biochemical aberrations in psoriasis of which we are aware. It is possible that these aberrations are of a serial nature, one following another in definite sequence. The initial biochemical alterations of psoriasis might be found by a study of patients with latent psoriasis. Difficulties of identifying a group of persons with latent psoriasis would be encountered but could be successfully met by carefully choosing young persons with a strong genealogic bent for psoriasis. Months or years later clinical psoriasis would develop in some members of such a group, thus giving evidence of their former latent status.

The development of clinical psoriasis is at times followed by complete remission. The shift from latent to clinical psoriasis usually heralds a persistent form which waxes and wanes in severity, but rarely shifts to the latent period. Less commonly in

the lifetime of an individual there are several shifts. Thus a person with psoriasis may show an initial transition from the latent to clinical phase, then a return to the latent phase for a time, and then clinical recurrence. These transitions are "natural" in that no medicinal agents bring them about. The natural evolution of clinical psoriasis often depends upon whether psoriasis becomes evident because of one of the "triggering stimuli" or whether it appears to develop spontaneously. If one or more stimuli are responsible, it may well be that correction or reversal of these will effect a change from a clinical to a latent phase. Such a change, which may be referred to as a remission, does not require medicinal agents. If known stimuli seem not to have been responsible, then the prognosis for nonmedicinal remission is quite poor.

In the light of our present knowledge there are a few other observed facts helpful in the predication and prognostication of psoriasis. Thus the earlier in life that psoriasis becomes clinically manifest, the poorer the prognosis for either spontaneous or therapeutic morbidistasis. A strong genetic background also generally suggests an unfavorable course.[1] Perhaps the form of psoriasis which may most often revert to a latent phase is the acute guttate variety following streptococcal infection. The diffuse psoriatic erythroderma is a variety that rarely clears completely.

THERAPEUTIC ALTERATIONS IN THE NATURAL HISTORY OF PSORIASIS

In this review of therapy, only agents that have a fairly consistent reproducible effect on psoriasis will be considered. These are: The folic acid antagonists, antimalarial drugs, adrenal corticosteroids and the Goeckerman regimen (the use of tar topically in conjunction with ultraviolet light therapy).

Folic acid antagonists

One of the actions of aminopterin is the blockage of the normal conversion of folic to folinic acid. Transmethylation reactions mediated by folinic acid are thus impaired and as a result the biosynthesis of purines and pyrimidines and consequently of nucleic acids is inhibited. The magnitude of such inhibition is correlated with the rate of the metabolic processes involving nucleic acid synthesis, and is thus great in the rapidly proliferating epidermal cells of psoriasis.[2,7,12,13]

While aminopterin reduces psoriasis by its cytotoxic action, it has not been observed to alter the natural history of psoriasis, for when it is discontinued psoriasis reappears as before. Its effect may be considered as suppressive to epidermopoiesis. The discontinuance of aminopterin usually results in a return of psoriasis to the pretreatment clinical state (Chart 6).

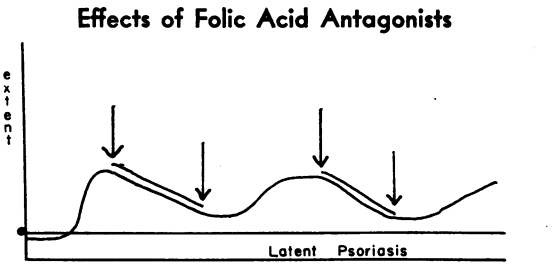

Chart 6.—The pattern of response to aminopterin as shown by one patient. Psoriasis recurred within a few weeks to pretreatment states following each course of therapy.

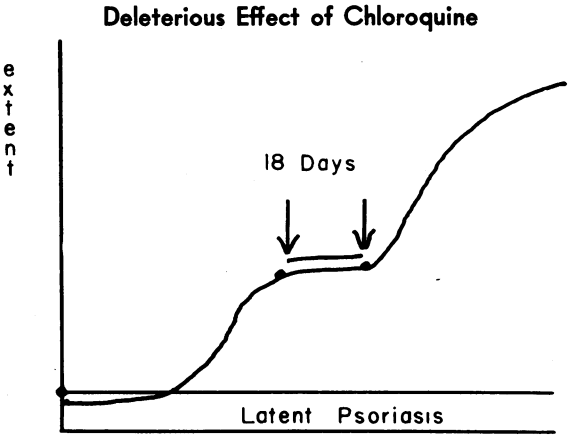

Chart 7.—Sudden spread of psoriasis due to antimalarial therapy.

Antimalarial drugs

The observations of Ziprkowski[19] concerning antimalarial agents and their effect on psoriasis have been substantiated by Sulzberger and Witten[18] and other investigators. Approximately 18 days after the initiation of atabrine or chloroquine therapy 75 per cent of patients with psoriasis will develop a severe generalized exfoliative psoriatic erythroderma (Chart 7). A small proportion of such patients may eventually have a clearing of the lesions for several weeks to several months. Even when this occurs, plaques of psoriasis tend to recur in the sites where they existed before the use of the antimalarial drugs. It is essential to know of the potential hazard of the antimalarial drugs, since many patients who receive them for the treatment of rheumatoid arthritis may also have psoriasis.

Adrenal corticosteroids

The injection of adrenal corticosteroids into plaques of psoriasis causes some plaques to thin out or resolve.[6] In some instances a brown macular patch with undesirable subcutaneous atrophy results

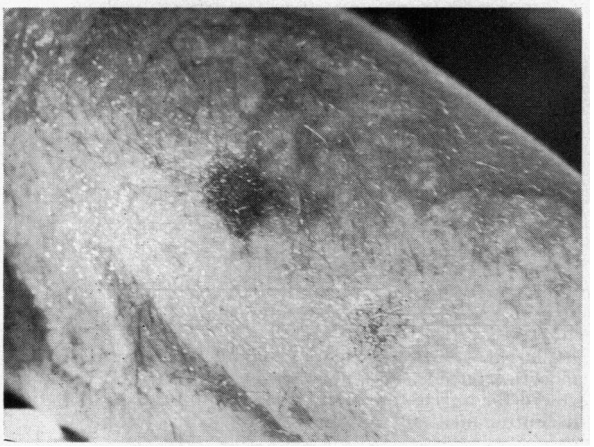

Figure 1.—Site of atrophy in a patch of psoriasis following intradermal corticosteroid injection.

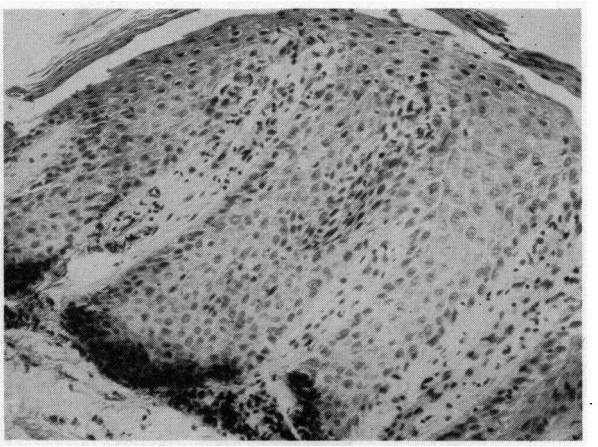

Figure 2.—Typical histopathologic appearance of psoriasis adjacent to intradermal corticosteroid injection site. Reduced from ×500.

(Figure 1). Figure 2 shows the typical histopathologic structure of a psoriatic lesion in a biopsy specimen taken from a site adjacent to the point of intradermal triamcinolone injection. Figure 3 shows psoriasis-free tissue taken from the site of injection of 1 cc. (25 mg.) of triamcinolone diacetate suspension diluted with an equal part of normal saline solution. Dermal atrophy also is shown. Such atrophy does not consistently occur, but it is unfortunately frequent. Intraplaque injection has a local morbidistatic effect for a time, "erasing" only the lesion treated. The natural course of the disease continues except for the particular locale or locales injected, and it may reactivate there later.

If corticosteroids are administered orally in sufficient amounts (generally 12 to 20 mg. initially per day with a daily maintenance dose of 4 to 12 mg. of triamcinolone or its equivalent) these agents are morbidistatic in action, reducing psoriasis in its clinical extent and severity.[4,16] On discontinuance, the eruption at times recurs in much the same magnitude as it existed before treatment. However, in about 50 per cent of the patients in whom such steroid therapy has been used there is a profound alteration in the natural course of psoriasis (Chart 8). The resultant poststeroid psoriasis may be far more extensive than that which existed before the use of the steroid; and it is often exudative and diffuse. Two varieties, both attended by extreme itching, have been observed, one being of guttate type and the other of exfoliative erythrodermic type (Figure 4). Biopsy of a lesion of the poststeroid-flared psoriasis (Figure 5) may not show the histopathologic structure that psoriasis usually shows. The characteristic microscopic features of psoriasis, such as suprapapillary thinning, regular acanthosis, clubbing of rete pegs, parakeratosis, dilated capillaries and occasional Munro abscess (Figure 2)

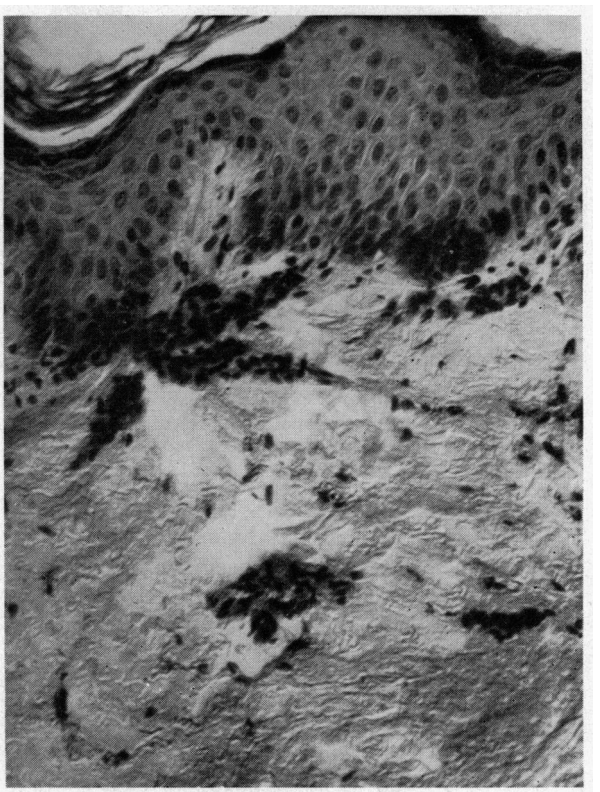

Figure 3.—Histopathologic features at site of intradermal corticosteroid injection. Reduced from ×200. Note the absence of pathologic features of psoriasis and dermal atrophy.

are not present. Instead there is a decided aggregation of inflammatory cells in the upper stratum Malpighii, spongiosis and irregular parakeratosis. There is also less evidence of suprapapillary thinning, of regular acanthosis or of capillary dilation. The person with steroid rebound psoriasis unfortunately faces a long, difficult and discouraging period during which no treatment is beneficial.

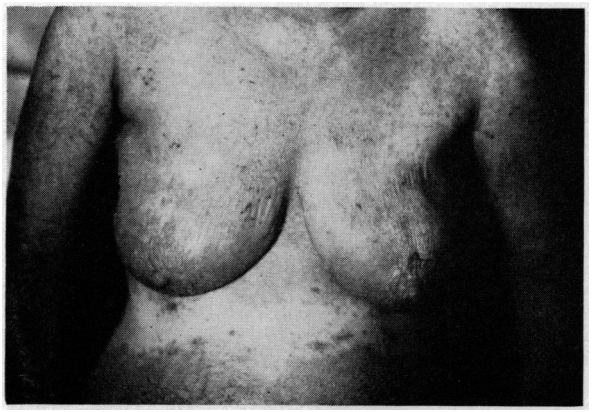

Figure 4.—The clinical appearance of severe diffuse eczematous psoriasis which may rebound following oral adrenocorticosteroids.

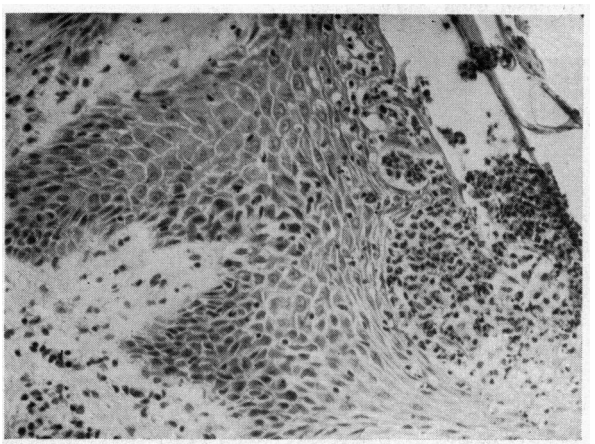

Figure 5.—Atypical histopathologic features occurring in poststeroid rebound psoriasis. Reduced from ×500.

The Goeckerman regimen

The treatment of psoriasis by use of the Goeckerman regimen has recently been surveyed in 50 patients treated on the Stanford Dermatology Service in the past two years. There are two distinct response patterns to the Goeckerman program (Charts 9 and 10).

The Goeckerman regimen brings about a gradual resolution of psoriasis. The individual lesions progressively regress, usually by the large lesions breaking up into smaller ones which subsequently fade. In about one-fourth of patients treated for three to five weeks there is a gradual recurrence of lesions after therapy is ended. In some three-fourths of patients the Goeckerman regimen results in resolution of almost all the lesions and is followed by a stable period during which no additional lesions or only a few appear for five to eighteen months, sometimes even longer. This response represents a striking alteration in the natural course of psoriasis by therapy.

Department of Dermatology, Stanford School of Medicine, 300 Pasteur Drive, Palo Alto (Farber).

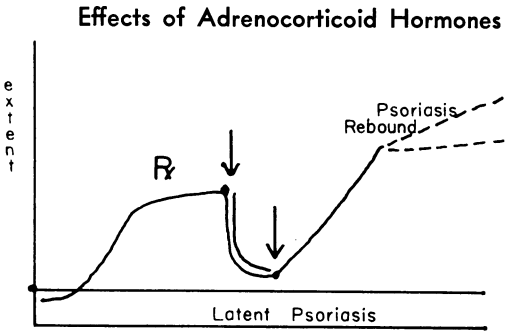

Chart 8.—Severe psoriasis rebound following oral adrenocorticosteroids. (Steroid therapy may have been administered for only a few weeks or sometimes for years before discontinuance and rebound.)

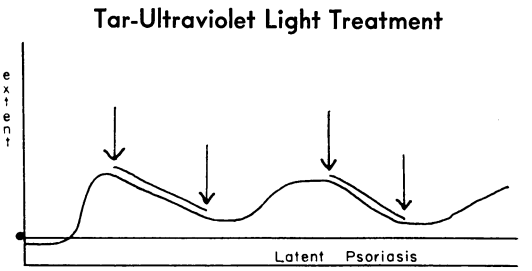

Chart 9.—Response to Goeckerman Therapy (tar-ultraviolet light) in 25 per cent of patients. The periods of therapy (distance between arrows) are generally three to eight weeks.

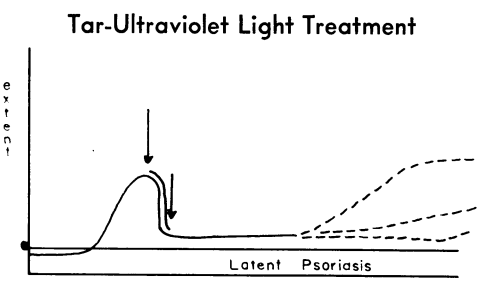

Chart 10.—Response to Goeckerman Therapy (tar-ultraviolet light) in 75 per cent of patients. (See text.)

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